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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/804,457	03/12/2001	Michael P. Maher	AUROBIO.026A	8759

20995 7590 10/02/2003

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EXAMINER	
MURPHY, JOSEPH F	

ART UNIT	PAPER NUMBER
1646	

DATE MAILED: 10/02/2003

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/804,457	MAHER ET AL.	
	Examiner	Art Unit	
	Joseph F Murphy	1646	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *15 April 2003* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

Formal Matters

Claims 1, 21 and 24 were amended in Paper No. 9, 4/15/2003. Claims 1-29 are pending and under consideration.

Response to Amendment

The rejection of claims 24-25 under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention has been obviated by Applicant's amendment and is thus withdrawn.

The rejection of claims 1-29 under 35 U.S.C. 103(a) as being unpatentable over Gonzalez et al. (1995) in view of Reiner et al. (1995), has been obviated by Applicant's amendment and is thus withdrawn.

Remaining issues, and new issues, are set forth below.

Specification

The objection to the Specification set forth in Paper No. 8, 10/21/2003 is maintained. If applicant desires priority under 35 U.S.C. 120 based upon a previously filed application, specific reference to the earlier filed application must be made in the instant application. For benefit claims under 35 U.S.C. 120, 121 or 365(c), the reference must include the relationship (i.e., continuation, divisional, or continuation-in-part) of the applications. This should appear as the first sentence of the specification following the title, preferably as a separate paragraph unless it appears in an application data sheet. The status of nonprovisional parent application(s) (whether patented or abandoned) should also be included. If a parent application has become a patent, the expression "now Patent No. _____" should follow the filing date of the parent application. If a

parent application has become abandoned, the expression "now abandoned" should follow the filing date of the parent application.

If the application is a utility or plant application filed under 35 U.S.C. 111(a) on or after November 29, 2000, the specific reference must be submitted during the pendency of the application and within the later of four months from the actual filing date of the application or sixteen months from the filing date of the prior application. If the application is a utility or plant application which entered the national stage from an international application filed on or after November 29, 2000, after compliance with 35 U.S.C. 371, the specific reference must be submitted during the pendency of the application and within the later of four months from the date on which the national stage commenced under 35 U.S.C. 371(b) or (f) or sixteen months from the filing date of the prior application. See 37 CFR 1.78(a)(2)(ii) and (a)(5)(ii). This time period is not extendable and a failure to submit the reference required by 35 U.S.C. 119(e) and/or 120, where applicable, within this time period is considered a waiver of any benefit of such prior application(s) under 35 U.S.C. 119(e), 120, 121 and 365(c). A priority claim filed after the required time period may be accepted if it is accompanied by a grantable petition to accept an unintentionally delayed claim for priority under 35 U.S.C. 119(e), 120, 121 and 365(c). The petition must be accompanied by (1) the reference required by 35 U.S.C. 120 or 119(e) and 37 CFR 1.78(a)(2) or (a)(5) to the prior application (unless previously submitted), (2) a surcharge under 37 CFR 1.17(t), and (3) a statement that the entire delay between the date the claim was due under 37 CFR 1.78(a)(2) or (a)(5) and the date the claim was filed was unintentional. The Director may require additional information where there is a question whether the delay was

unintentional. The petition should be addressed to: Mail Stop Petition, Commissioner for Patents, P.O. Box 1450, Alexandria, Virginia 22313-1450.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-21 are rejected under 35 U.S.C. 102(b) as being anticipated by Sinha et al. (1995).

Sinha et al. developed a system for simultaneous optical recording of transients of membrane potential and intracellular calcium concentration from mammalian brain slice preparations with high spatio-temporal resolution. In the method of Sinha et al. simultaneous recording was achieved by using two dedicated photodetectors together with two fluorescent indicators. Specifically, the calcium-sensitive dye Calcium Orange and the voltage-sensitive dye RH-414 were used because they have overlapping excitation spectra, but separable emission spectra. The method of Sinha et al. anticipates claims 1 and 21 because the method uses cells (specifically, hippocampal slices, see page 53), the cells are exposed to a compound (the glutamate antagonists CNQX and d-APV, see page 56, Figure 5), and the cells are exposed to an electric field without using a patch clamp (in this instance an a single stimulus is delivered via an electrode to the stratum radiatum area. N.b. this is not a patch clamp set-up since the electrode is a tungsten stimulation electrode and is used to induce an electric field potential which induces the cellular response, but does not make use of the patch clamp technique wherein a glass pipette

filled with a solution which contains ionic salts is in contact with the interior of the cell.). The method of Sinha also measures transmembrane potential without using the patch clamp technique because the cells are loaded with dyes sensitive to transmembrane potential, and the fluorescence is measured (see page 56, Figure 5), thus claims 1, 2 and 21 are anticipated. Claims 3 and 4 are anticipated because the current pulses will not cause electroporation, claims 5-10 are anticipated because the cells comprise a voltage gated ion channel which will be released from inactivation in response to the stimulation, and the measuring was done using a transmembrane potential dye. Claims 11-20 are anticipated because the responses are stimulated with 500 micro sec current pulses delivered at frequencies less than 0.05 Hz (page 53, column 2, last paragraph).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-29 are rejected under 35 U.S.C. 103(a) as being unpatentable over WO 96/41166 (Tsien et al.).

Tsien et al. teaches methods of assaying for small changes in transmembrane potential using voltage sensitive dyes (page 3, lines 1-25). Tsien et al. teach methods of screening for potential therapeutic drugs that affect membrane potentials in living cells (page 42). Tsien et al. further teach the use of cells which have been transfected with nucleic acids encoding, *inter alia*, ion channels (page 44, lines 1-5). Tsien et al. further teaches the use of cell lines including HEK293, LM(TK-), COS, and CHO cells (page 44, lines 7-11). Tsien et al. teaches that the transfected cells are treated with a stimulus that modulates the ion channel (page 43, lines 15-20). Tsien et al. teaches that the ion channel may be a sodium, potassium, or calcium channel, which may be voltage-gated (page 43, lines 27-31). While Tsien et al. does not set forth the stimualtion protocols it is a designer's choice to use an electric field to stimulate the ion channel, given that it is known in the art to use electric fields to stimulate voltage gated ion channels, as shown in Jacobs et al. Jacobs et al. teaches the electric field stimulation of cultured cells to stimulate Ca++ transients (see page 4130, column 1, second paragraph and page 4131, Figure 1). Thus it would have been obvious to one of skill in the art at the time the invention was made to practice a method of assaying a compound agent for activity against an ion channel wherein a cell line is transfected with the ion channel of interest, and the cells are activated with an electric field, and the transmembrane potential is measured without the use of a patch clamp. The motivation is provided in the Tsien et al. reference that teaches that the method is sensitive to mall changes in transmembrane potentials, and can respond on a rapid, millisecond timescale to changes in membrane potentials (page 2, lines 30-38).

Conclusion

No claim is allowed.

Advisory Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joseph F. Murphy whose telephone number is 703-305-7245. The examiner can normally be reached on M-F 7:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Yvonne Eyler can be reached on 703-308-6564. The fax phone numbers for the organization where this application or proceeding is assigned are 703-305-3014 for regular communications and 703-308-0294 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0196.

Joseph F. Murphy, Ph. D.
Patent Examiner
Art Unit 1646
September 29, 2003

YVONNE EYLER, PH.D
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600